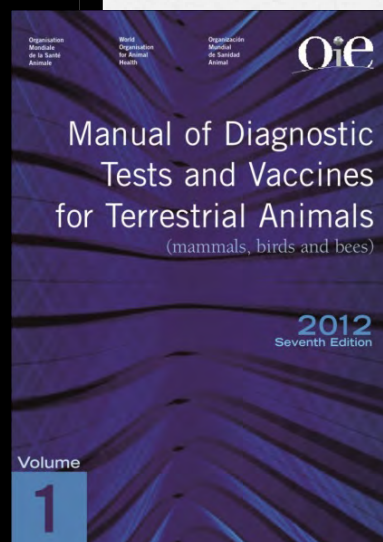


# The OIE Manual of Diagnostic Tests and Vaccines for Terrestrial & Aquatic Animals

VMP Focal point training  
MAPUTO

3 – 5 December 2013



*Dr Susanne Münstermann  
Scientific and Technical Department*



- o The OIE Specialist Commissions and their mandate
  
- o The Terrestrial Manual - overview
  - o Diagnostic Tests
  - o Vaccines
  
- o The Aquatic Manual - overview
  - o Diagnostic Tests
  - o Vaccines

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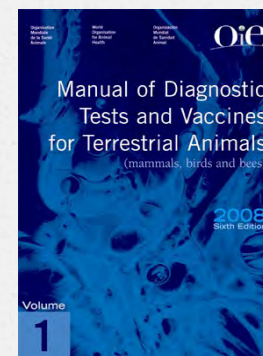
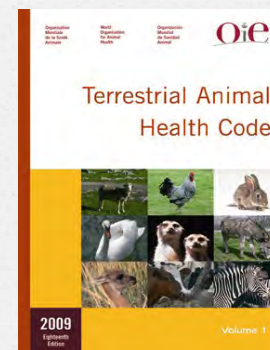
*Terrestrial Animal Health Code – mammals, birds and bees*

*Aquatic Animal Health Code – fish, molluscs and crustaceans*

*Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*

*Manual of Diagnostic Tests for Aquatic Animals*

*OIE Quality Standard and Guidelines for Veterinary Laboratories: Infectious Diseases*



# Specialist Commissions

**Terrestrial Animal Health Standards Commission**  
**"Code Commission"**

**Scientific Commission for Animal Diseases**  
**"Scientific Commission"**

**Biological Standards Commission**  
**"Laboratories Commission"**

**Aquatic Animal Health Standards Commission**  
**"Aquatic Animals Commission"**

# Biological Standards Commission

## "Laboratories Commission"

- Six Members elected by the World Assembly of Delegates for a 3-year term (e.g. 2012)
- Approves **OIE Reference Laboratories/OIE Collaborating Centres/Laboratory Twinning**
- Provides scientific advice for Standards related to diagnostics for eventual inclusion in the *Terrestrial Code*
- **Develops and sets International laboratory standards – diagnostics, vaccines, etc. (*Terrestrial Manual*)**
- Promotes the preparation and distribution of reagents

# Putting faces to names

The screenshot shows a web browser window displaying the OIE website. The URL in the address bar is <http://www.oie.int/en/international-standard-setting/specialists-commissions-groups/laboratories-commission-reports/commission-members-d...>. The page title is "Commission - Member's d...". The OIE logo is visible at the top left, and the navigation menu includes "Home", "About us", "Our scientific expertise", "Support to OIE members", "Animal health in the World", "International Standard Setting", "Animal welfare", "One Health", and "Publications and documentation". The main content area is titled "Members' details" and lists six members with their photos, names, titles, and contact information.

Name	Title	Contact Information
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<http://www.oie.int/en/international-standard-setting/specialists-commissions-groups/laboratories-commission-reports/commission-members-details/>

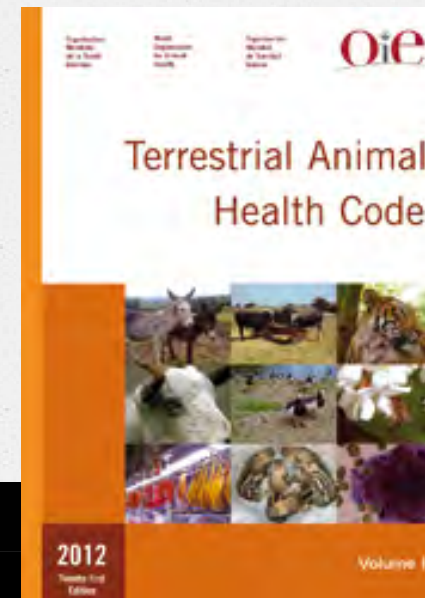


# *Terrestrial Manual*

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## Overview

- Describes internationally agreed laboratory **standard** methods for disease **diagnosis**, and
  - Describes also, when relevant, the requirements the production and control of **vaccines** and other biological products
- **Is the companion volume to the *Terrestrial Animal Health Code***

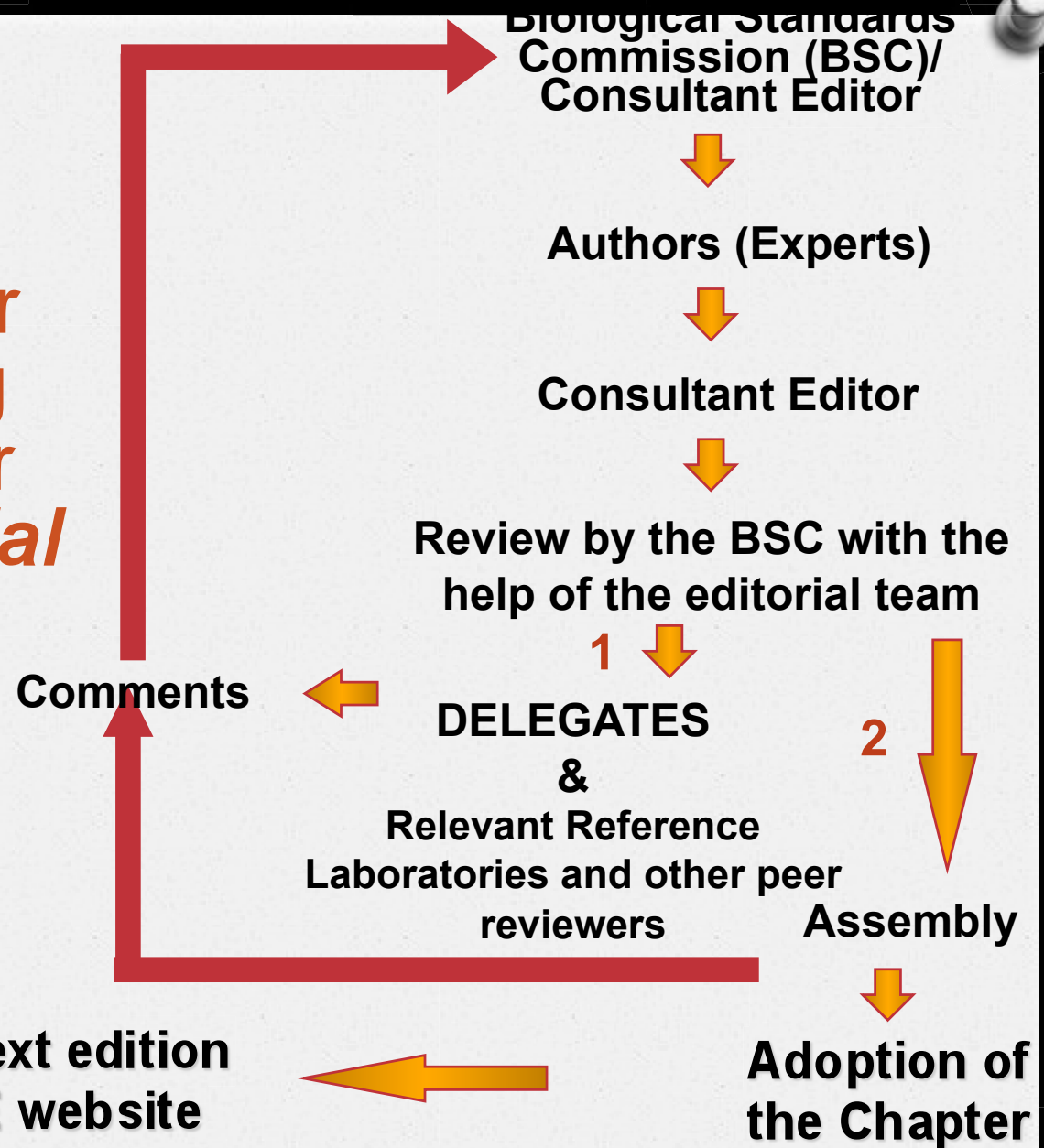




- First published in 1989 and since then every 4 years in paper version.
- The last printed version is the 2012, 7<sup>th</sup> edition
- Available on the OIE website – includes all updated chapters:

<http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/>

# General Process for developing Chapter for the *Terrestrial Manual*



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o Minimum requirements for vaccine production facilities

o Quality control of vaccines

→ your role in providing expert opinion is crucial!

# Structure

Divided into different parts :

- **Part 1:** 10 introductory chapters on general issues of interest to veterinary laboratories
- **Part 2:** 113 Chapters on specific diseases (OIE listed diseases and other diseases of public health or trade importance)
- **Part 3:** General Guidelines
- **Part 4:** OIE Reference Experts and disease index

# Structure

## Part 1 – Introductory chapters:

- 1.1.1. Collection, transmission and storage of diagnostic specimens (13)
- 1.1.2. Transport of specimen of animal origin (13)
- 1.1.3. Biosafety and biosecurity in the veterinary diagnostic microbiology laboratory and animal facilities
- 1.1.4. Quality management in veterinary testing laboratories
- 1.1.5. Principles and methods of validation of diagnostic assays for infectious diseases (13)
- 1.1.6. Principles of veterinary vaccine production (including diagnostic biologicals)

# Structure

## Part 1 – Introductory chapters (contd):

1.1.7. Tests for sterility and freedom from contamination of biological materials

1.1.8. *Minimum requirements for vaccine production facilities (under study)*

1.1.9. *Quality control of vaccines (under study)*

1.1.10. International standards for vaccine banks

# Structure

**Part 2 – 113 Chapters on specific diseases:**

OIE listed diseases + other diseases of global importance:

Subdivided by:

- Multiple species (3)
- Apidae (3)
- Aves
- Bovidae (2)
- Equidae (6)
- Leporidae
- Ovidae and Caprinae (2)
- Suidae (1)
- Other Diseases (1)

(x) = updated in 2013

# Structure

## Part 3 – General Guidelines

- 4.1 Laboratory methodologies for bacterial antimicrobial susceptibility testing \*
- 4.2 Biotechnology in the diagnosis of infectious diseases \*
- 4.3 The application of biotechnology to the development of veterinary vaccines
- 4.4 The role of official bodies in the international regulation of veterinary biologicals

\* Approved in May 2012



# Structure

**Part 2** – Chapters on specific diseases:

Each disease chapter (except FMD) is developed following this template:

- Summary
- A. Introduction
- B. Diagnostic techniques
- C. Requirements for vaccines and diagnostic biolog
- References



**OIE *Terrestrial Manual*  
and  
Diagnostic tests**

Relevant parts in the *Terrestrial Manual*:

- Several **introductory chapters** of the *Terrestrial Manual* are relevant for diagnostic tests.
- Considering the importance to validate diagnostic tests, the introductory chapters on the **general principles for the validation of diagnostic assays (1.1.5)** are of special interest.
- In each disease-specific chapter, the **Part B** is on the diagnostic techniques and provides detailed descriptions of the **prescribed** and alternative tests.



Three possible categories of tests described in the part B of the disease-specific chapters:

1. Prescribed tests,
2. Alternative tests, and
3. Other tests

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- **Prescribed tests** are required by the *Terrestrial Code* for the testing of animals before they are moved internationally.
- Printed in **blue** in the relevant disease-specific chapters.
- All the prescribed tests are listed in the table: « *list of tests for international trade* », page XI in each of the two volumes.

- **Alternative tests** are suitable for the diagnosis of disease within a local context, and can also be used in the import/export of animals after bilateral agreement.
- The alternative tests are also listed in the table:  
« *list of tests for international trade* », page XI in each of the two volumes.

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- There are often **other tests** described in the chapters, which may also be of some practical value in local situations or which may still be under development.

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*Table 1. Test methods available for the diagnosis of equine infectious anaemia and their purpose*

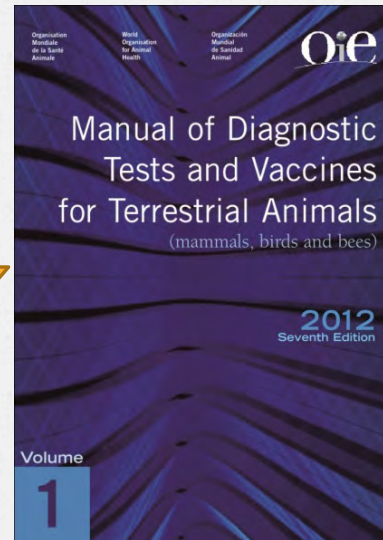
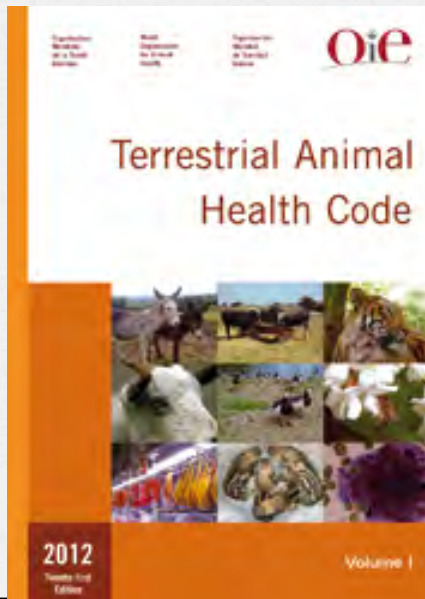
Method	Purpose			
	Population freedom from infection/ efficiency of eradication policies	Individual animal freedom from infection	Confirmation of clinical cases	Prevalence of infection – surveillance
Agar gel immunodiffusion	++	++	++	++
Enzyme-linked immunosorbent assay	++	++	+	+
Immunoblot	-	++	++	-
Polymerase chain reaction	-	+/-	+	-
Virus isolation/horse inoculation	-	-	+	-

Key: +++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; - = not appropriate for this purpose.  
Although not all of the tests listed as category +++ or ++ have undergone formal standardisation and validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.

Example: Equine Infectious Anaemia



Where the *Terrestrial Code* requires that tests are carried out for international movement, the *Terrestrial Manual* should provide a recommended laboratory method.





**OIE *Terrestrial Manual*  
and  
Vaccines**

Relevant parts in the *Terrestrial Manual*:

- o Several *introductory chapters* of the *Terrestrial Manual* are relevant for the vaccines (production and quality) and more will be developed.
- o Chapter 1.1.6, *Principles of Veterinary Vaccine Production* is of special interest.
- o In the relevant *disease-specific chapters*, the **Part C** is on the Requirements for Vaccines and Diagnostic Biologicals – several diseases have just been reviewed, e.g. FMD, Rabies, CSF, RVF



## Summary of the content:

- o Nomenclature: for this chapter, the term “vaccine” includes “all products designed to stimulate active immunisation of animals against disease, without regard to the type of microorganism or microbial toxin from which they may be derived or that they contain”
- o Quality Assurance / Production facilities & the importance of their inspection / Master Seed & Master Cell Stocks / Ingredients / Consistency of Production / Safety & Efficacy Tests / Batch/serial release for Distribution / Labelling / Biotechnology-derived vaccines

## Summary of the content (contd):

Two appendixes:

1. Risk analysis for biologicals for veterinary use (provides only general considerations)

3. Risk analysis for veterinary vaccines:

Introduction – Principles – Manufacturing practices –  
Registration in the importing country – Categorisation of  
veterinary vaccines – Vaccinovigilance – Risk communication

**General Template of the Part C which was used until now and is still present in some disease-specific chapters**

1. Seed Management



- a) Characteristics of the seed
- b) Method of culture
- c) Validation as a vaccine

2. Method of Manufacture

3. In-process control

4. Batch control



- a) Identity
- b) Sterility
- c) Safety
- d) Potency
- e) Duration of protection
- f) Stability
- g) Preservatives
- h) Precautions

5. Tests on the final product

- a) Safety
- b) Potency



## 1. Background

- o Availability, rationale, intended use

## 2. Outline of production and minimum requirements for vaccines

### a) Characteristics of the seed

- a) Biological criteria
- b) Quality criteria
- c) Validation of the vaccine strain

### b) Method of manufacture

- o Procedure
- o Requirements for ingredients
- o In process controls
- o Final product batch tests

### c) Requirements for registration

- o Manufacturing process
- o Safety requirements
- o Efficacy requirements
- o Potency requirements

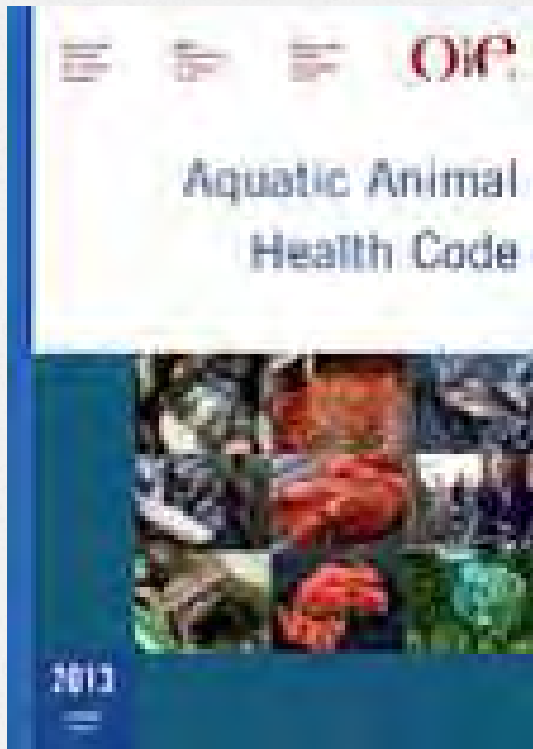
## 3. *Specific topics (e.g. oral vaccine)*

### Implemented for

- FMD
- Rabies
- CSF



# The Aquatic Animal Health Code



- o **Objective:** a uniform approach to the diagnosis of aquatic diseases listed in the Aquatic **Code**
- o Diagnostic tests are used to comply with standards for international movement / trade of aquatic animals
- o Manual is produced every 1 - 2 years, updates are on-line
- o Available in English and Spanish



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- o Unlike terrestrial animals, crustaceans, amphibians, fish and molluscs don't often show specific clinical disease signs
- o Therefore the best suited diagnostic is detection of the **pathogen**
- o The methods are mainly **direct**, indirect methods, e.g. antibody detection, are generally not accepted

- o Molluscs and crustaceans don't produce antibodies
- o General approach: pathogen isolation and identification, or
- o Antigen detection by immunological or molecular techniques
- o PCR is recommended for detection and confirmation but not for screening to prove absence of disease



Divided in two parts:

- **Part 1:** 3 chapters of general interest for veterinary laboratories
  
- **Part 2:** specific diseases
  - Amphibians: 2 diseases
  - Crustacéans: 10 diseases (3 new in 2012)
  - Fish: 11 diseases (2 new in 2012)
  - Molluscs: 9 diseases (2 new in 2012)

- o Quality management in veterinary testing laboratories
- o Principles and methods of validation of diagnostic assays for infectious diseases
- o Methods for disinfection of aquaculture establishments



The chapters of Part 2 follow this **structure**:

- o Scope
- o Disease information
- o Sampling
- o Diagnostic methods
- o **Rating of tests against purpose of use**
- o Tests recommended for the declaration of disease freedom
- o Corroborative diagnostic criteria



*Table 5.1. Methods for targeted surveillance and diagnosis*

Method	Targeted surveillance				Presumptive diagnosis	Confirmatory diagnosis
	Ova/milt	Fry/fingerlings	Juveniles	Adults		
Gross signs	na	d	d	d	d	d
Histopathology	na	d	d	d	b	d
Immunoperoxidase stain	na	c	c	c	c	c
Transmission EM	na	d	d	d	c	b
Immuno-EM	na	d	d	d	c	b
Cell culture	na	a	a	a	a	b
Antigen-capture ELISA	na	a	a	a	a	a
Antibody-capture ELISA	na	d	d	c	c	d
PCR-REA	na	d	a	d	c	a
PCR sequence analysis	na	d	d	d	c	a



Thank you for your attention

Oie

